

REMARKS

Claims 1, 3, 7-15, and 17-47 were pending in the application. Claims 10-14, 18, 21, and 23-45 have previously been withdrawn. Claims 2, 4-6, and 16 have previously been canceled. Claims 20 and 46-47 have been canceled herein. Upon entry of the present amendment, claims 1, 3, 7-15, 17-19, 21, and 22-45 are pending, with claims 1, 3, 7-9, 15, 17, 19, and 22 under examination. Support for the amendments to claims 1 and 22 may be found, for example, at page 8, lines 10-11. No new matter has been added.

Amendment of the claims or cancellation of any claims should in no way be construed as an acquiescence, narrowing, or surrender of any subject matter. The amendments are being made not only to point out with particularity and to claim the present invention, but also to expedite prosecution of the present application. Applicant reserves the option to prosecute the originally filed claims further, or similar ones, in the instant or subsequently filed patent applications.

Objection Withdrawn

Applicant gratefully acknowledges the withdrawal of the objection to the drawings, in view of the submission of replacement drawings on July 18, 2007.

Rejection of Claims 1 and 3¹ Under 35 U.S.C. § 102(e)

Claims 1 and 3 stand rejected under 35 U.S.C. § 102(e), as allegedly anticipated by Bonjouklian *et al.* (U.S. Patent No. 5,504,103), as evidenced by Liu *et al.* (Current Opinion in Immunol., 1992, 4: 265-270). In the previous Office Action (mailed January 18, 2007), the Examiner contends that Bonjouklian *et al.* discloses a method of administering a wortmannin analog to a mammal. In the instant Office Action, the Examiner maintains the rejection, and cites Liu *et al.* as allegedly providing support for the contention that activated T cells are intrinsically present in the immune system.

¹ The Examiner has cited claims 1-6 in the rejection; however, claims 2, and 4-6 have been previously canceled.

Applicant respectfully traverses the rejection. However, solely in order to expedite prosecution of the application, and in no way conceding the validity of the Examiner's rejection, Applicant has amended claim 1 to recite that the inhibition of a T cell be performed "*in a subject in need thereof*". Among other discoveries, Applicant has discovered that inhibition of phosphatidylinositol 3-kinase (PI3K) in a T cell can inhibit T cell responses, such as lymphokine production and cellular proliferation. This was not recognized by Bonjouklian *et al.*, which discloses analogs of wortmannin and is devoid of any teaching of an ability to inhibit a T cell response and, in fact, any exemplification demonstrating activity in any biological assay. While Bonjouklian *et al.* provide a non-enabling disclosure of a number of potential indications for which the wortmannin analogs may be used (col. 6, li. 1-19), inhibiting T cell activation in a subject in need thereof is not among them. In fact, upon reviewing the disclosure of Bonjouklian *et al.*, it is apparent that Bonjouklian *et al.* only recognized the utility of their wortmannin analogs in the treatment of cancer, and not inhibition of T cell activation, as evidenced by the following statements:

"PI 3-kinase appears to be an important enzyme in signal transduction, with particular implications relative to mitogenesis and the malignant transformation of cells" (col. 2, li. 14-15, *emphasis added*)

"[T]he present invention provides a method for treating phosphatidylinositol 3-kinase-dependent conditions, particularly neoplasms" (col. 2, li. 34-36, *emphasis added*)

"[A]n especially preferred embodiment of the present invention includes a method of treating phosphatidylinositol 3-kinase-dependent neoplasms, particularly various lymphosarcomas, with a compound of formula I. Other PI 3-kinase-dependent neoplasms include, for example, adenocarcinoma of the female breast, colon cancer, epidermal cancers of the head and neck, leukemia, melanoma, ovarian carcinoma, plasma cell myeloma, and squamous or small-cell lung cancer."

Moreover, the only disease that is recited in the claims is "a neoplasm" (claim 13). When considered in light of the fact that Applicant was the first to discover that inhibition of PI3K can inhibit T cell responses, it is very clear that Bonjouklian *et al.* never envisioned the use of wortmannin analogs for inhibiting a T cell response. In fact, a person of ordinary skill in the art would recognize that the inhibition of a T cell response would be undesirable in the context of treating a neoplastic condition. Bonjouklian *et al.*, therefore, does not teach or suggest amended claim 1 but, in fact, teaches away from the now claimed method "for inhibiting T cell activation in a subject in need thereof". Claims 1 and 3 are, therefore, novel and non-obvious over

Bonjouklian *et al.* and Liu *et al.*, either alone or in combination. Applicant, therefore, respectfully requests reconsideration and withdrawal of the rejection.

***Rejection of Claims 15, 17, 19-20, and 22² Under 35 U.S.C. § 112, First Paragraph:
Enablement***

The Examiner has rejected claims 15, 17, 19-20, and 22 under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled by the specification. Specifically, the Examiner contends that the specification

does not reasonably provide enablement for claims directed to a method of inducing unresponsiveness to an antigen in a T cell and further administering the T cell to a subject suffering from an autoimmune disease.

Applicant respectfully traverses the rejection. However, solely in order to expedite prosecution of the application, and in no way conceding the validity of the Examiner's rejection, Applicant has canceled claim 20 and amended claim 22 to depend from claim 1, rendering the Examiner's rejection over "administering the T cell to a subject" moot.

With respect to the induction of antigen-specific unresponsiveness, Applicant respectfully points out that it is well-recognized that presentation of an antigen in the absence of costimulatory activity, or the presence of agents that inhibit a costimulatory signal, leads to the development of tolerance. This is shown, for example, in Figure 1 of Liu *et al.*, cited by the Examiner in the instant Office Action. Moreover, the literature is replete with examples of the induction of tolerance by blocking costimulatory activity. One of ordinary skill in the art would, therefore, readily recognize that the agents of the instant methods, which block costimulatory activity by inhibiting PI3K, would antigen-specific unresponsiveness. Reconsideration and withdrawal of these rejections is, therefore, respectfully requested.

Rejection of Claims 1, 3, 7-9³ Under Nonstatutory Obviousness-Type Double Patenting

Claims 1, 3, and 7-9 stand rejected on the grounds of nonstatutory obviousness-type double patenting, as allegedly being unpatentable over claims 1-4 and 7-10 of U.S. Patent No.

² The Examiner has cited claims 15-17, 19, 20, and 22 in the rejection; however, claim 16 has been previously canceled.

6,632,789 (June). Applicant respectfully requests that the Examiner hold all nonstatutory obviousness-type double patenting rejection in abeyance, until allowable subject matter is determined. Upon determination of allowable subject matter, Applicant may consider the filing of a terminal disclaimer.

Conclusion / Finality of the Office Action

In justifying the issuance of the Final Office Action, the Examiner refers to the “Applicant response filed on 10-06-2006” (page 7 of the Office Action). Applicant did not file a response on October 6, 2006, and the instant Office Action should be in response to Applicant’s Amendment and Response filed July 18, 2007 and Response to Notice of Non-Compliant Amendment filed September 27, 2007. Acknowledgement and appropriate correction is requested.

³ The Examiner has cited claims 1-6 in the rejection; however, claims 2, and 4-6 have been previously canceled.

CONCLUSION

Early and favorable consideration of the application is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at (617) 832-1000. If any fees are due, the Commissioner is hereby authorized to credit any overpayment or charge any deficiencies to **Deposit Account No. 06-1448, WYS-014.02.**

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Respectfully submitted,

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